REMARKS

Claims 10-14 have been rejected under 35 U.S.C. §101 as being directed to non-statutory subject matter. Claims 10-14 have been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirements, as set out in specific remarks made by the Examiner. Claims 10-14 also have been rejected under 35 U.S.C. §112, first paragraph, as not being enabling to make and/or use the invention commensurate in scope with the claims. Claims 10-14 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite for reasons specified by the Examiner. Finally, the disclosure is objected to for informalities alleged by the Examiner.

Referring first to the objection by the Examiner, applicant has amended the claims to comply with the Examiner's remarks.

With respect to the rejection under 35 U.S.C. §112, second paragraph, applicant has amended Claim 10 to remove the step to "iterate" the process. Iteration is at the option of the operator and may not be needed since the density map modification may be adequate after a single pass.

Applicant respectfully traverses the rejection of the claims under 35 U.S.C. §101 as directed to non-statutory subject matter. The Examiner remarks that the process manipulates electron density data "without resulting in any physical transformation outside of a computer or other computational device." As noted in MPEP 2106.IV.B.2.(b).(i), a process is clearly statutory "it if requires physical acts to be performed outside the computer . . . . But, "[i]f a claim does not clearly fall into one or both of the safe harbors, the claim may still be statutory if it is limited to a practical application in the technological arts." The next section of MPEP provides an example: ". . .a computer process that simply calculates a mathematical algorithm that models noise is nonstatutory. However, a claimed process for digitally filtering noise employing a mathematical algorithm is statutory." Applicant's claimed process is the application of mathematical algorithms to modify "an electron density map of an experimental crystal structure," as recited in the preamble of Claim 10. This is clearly a "practical application in the technological arts" and constitutes statutory subject matter under 35 U.S.C. §101.

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To more clearly recite this function, the step of forming a revised electron density map from a new set of calculated structure factors is recited. The rejection of Claims 10-14 as being directed to nonstatutory subject matter should be withdrawn.

Applicant has also amended Claim 10, step (a), to recite that the model electron density map is formed from an exemplary model crystal structure having known crystallographic information. Support for this amendment is found in the specification at page 15, lines 1-14. This amendment clarifies that the process is directed to processing crystallographic data.

Applicant has amended Claim 10, step (g), to overcome the rejection under 35 U.S.C. §112, first paragraph. The Examiner has commented that the practice of log-likelihood determination of step (g) of claim 10, as set out in the specification at page 12, lines 2-7, is enabling for the practice of the specific log-likelihood determination, but does not provide enablement for a "generic" log-likelihood determination. Amended step (g) incorporates the log-likelihood function as presented at page 12, lines 2-7.

Applicant respectfully traverses the rejection of Claims 10-14 under 35 U.S.C. §112, first paragraph, as not enabled by applicant's specification. The PTO has the burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification. See In re Wright, 27 USPQ2d 1510 (Fed. Cir. 1993). The reasons cited by the Examiner are:

1. "It is noted that the electron densities of proteins is a complex concept with well known complexities of electron orbital theory and/or quantum mechanical representations of electron wave/particle characteristics . . . ."

2. "[T]he results of experiments in genetic engineering are unpredictable."

While these statement may be true, they are unrelated to the claimed invention. Claims 10-14 are directed solely to "A method for improving an electron density map . . . ." from an initial experimental electron density map, taught by applicant to result from x-ray crystallographic data. The PTO has failed to establish a reasonable explanation for believing applicant's disclosure is not enabling.

Further, a patent application is not required to teach that which is well known to a person skilled in the art.

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"Requiring inclusion in the patent of known scientific/technological information would add an imprecise and open-ended criterion to the content of patent specifications, could greatly enlarge the content of patent specifications and unnecessarily increase the cost of preparing and prosecuting patent applications, and could tend to obfuscate rather than highlight the contribution to which a patent is directed. A patent is a not a scientific treatise, but a document that presumes a readership skilled in the field of the invention."
Ajinomoto Co., Inc. v. Archer-Daniel-Midland Co., 56 USPQ2d 1332, 1338 (Fed. Cir. 2000).

All of the information needed to practice applicant's claimed invention is publicly available, as shown by the numerous citations in applicant's specification and is not required to be included in the patent application to provide an enabling disclosure to persons skilled in the art.

A Declaration Under 37 C.F.R. 1.132 from Dr. Li-Wei Hung is attached to respond to the statements made by the Examiner in rejecting the claims. Dr. Hung is a person of ordinary skill in the art of protein crystallography and is also qualified to address the issue of undergraduate and graduate studies with respect to the general knowledge of graduates regarding the algorithms used in applicant's claimed process.

Referring to the factors used by the Examiner in asserting a lack of enablement, applicant responds as follows:

1.   Quantity of experimentation necessary - no experimentation is required since the process uses data generated from routine protein crystallography, i.e., numerical values of electron density values in a three-dimensional matrix (Hung Declaration, paragraph 4).

2.   The amount of direction presented - Dr. Hung sets out the relevant portions of the specification for each of the issues raised by the Examiner, analyzes the required knowledge and teaching of the specification, to arrive at the conclusion that a person of ordinary skill in the art of protein crystallography could carry out the process.

3.   The presence or absence of working examples - Exemplary crystallographic and electron density map structures and values are taught at pages 19-21 and Figures 3A-D.

4.   The nature of the invention - The invention is directed to applying known mathematical algorithms to conventional protein crystallographic information in order to

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obtain a modified electron density map that is believed to better represent the protein crystal structure.

5. The state of the prior art - As discussed in the patent application, there have been numerous processes that apply various mathematical techniques to improve the quality of electron density maps derived from protein crystallographic data. Applicant has added a maximum-likelihood approach to this prior art to add known information to experimental information to increase the overall likelihood of an electron density map.

6. The relative skill of those in the art - As noted by the Examiner, the level of skill in molecular biology is high; declarer Li-Wei Hung considers that he represents a person of ordinary skill in the art of protein crystallography and he has a PhD in biophysics.

7. The predictability or unpredictability of the art - The process is highly predictable since actual experimental results are being manipulated by well known algorithms. There may be unpredictability in a subsequent interpretation of the results, but not in obtaining the results.

8. The breadth of the claims - Applicant's claims are limited to the application of specific mathematical algorithms to experimental protein crystallographic data.

In view of the Declaration of Li-Wei Hung that clearly establishes facts leading to the conclusion that a person of ordinary skill in the art of protein crystallography could practice the claimed invention as taught by the application specification without undue experimentation, the Examiner is respectfully requested to withdraw the rejection of Claims 10-14 under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. MPEP 2106.V.B.2. provides an example of an adequate teaching for "a programmed computer that determines and displays the three dimensional structure of a chemical compound . . . ." The disclosure must

> "-enable a person skilled in the art of molecular modeling to understand and practice the underlying molecular modeling processes; and
>
> - enable a person skilled in the art of computer programming to create a program that directs a computer to create a program that directs a computer to create and display the image representing the three-dimensional structure of the compound."

Dr. Hung's Declaration clearly establishes that the disclosure enables a person skilled in the art of protein crystallography to understand the disclosed process, and shows

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that commercial programs are available to perform the claimed mathematical algorithms. Both conditions are satisfied by applicant's disclosure.

The Examiner is respectfully requested to allow Claims 10-14, as amended, and to pass this case to issue.

Applicant's attorney would be pleased to discuss any of these issues with the Examiner by telephone if the Examiner concludes such a discussion would assist in placing this case in condition for allowance.

Respectfully submitted,

Date: _Oct. 9, 2003_

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